

Claims:

1. A method for detecting a colon cancer in a subject in need thereof, comprising:
 - determining the expression level of at least 14 biomarkers from a test sample from the subject by contacting the test sample with a plurality of agents specific to detect the expression of the at least 14 biomarkers, wherein the 14 biomarkers comprise *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, *UMPS*, and a housekeeping gene;
 - normalizing the expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS*;
 - inputting each normalized expression level into an algorithm to generate a score;
 - comparing the score with a predetermined cutoff value; and
 - identifying the presence of a colon cancer in the subject when the score is equal to or greater than the predetermined cutoff value or identifying the absence of a colon cancer in the subject when the score is less than the predetermined cutoff value.

2. A method for determining whether a colon cancer in a subject is stable or progressive, the method comprising:
 - determining the expression level of at least 14 biomarkers from a test sample from the subject by contacting the test sample with a plurality of agents specific to detect the expression of the at least 14 biomarkers, wherein the 14 biomarkers comprise *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, *UMPS*, and a housekeeping gene;
 - normalizing the expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS*;

inputting each normalized expression level into an algorithm to generate a score;
 comparing the score with a predetermined cutoff value; and
 identifying that the colon cancer in the subject is progressive when the score is
 equal to or greater than the predetermined cutoff value or identifying that the colon
 cancer in the subject is stable when the score is less than the predetermined cutoff value.

3. A method for determining the completeness of surgery in a subject having a colon cancer,
 the method comprising:

determining the expression level of at least 14 biomarkers from a test sample from
 the subject after the surgery by contacting the test sample with a plurality of agents
 specific to detect the expression of the at least 14 biomarkers, wherein the 14 biomarkers
 comprise *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*,
SNRPA, *SORD*, *STOML2*, *UMPS*, and a housekeeping gene;

normalizing the expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*,
HMOX2, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS* to the
 expression level of the housekeeping gene, thereby obtaining a normalized expression
 level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*,
S100P, *SNRPA*, *SORD*, *STOML2*, and *UMPS*;

inputting each normalized expression level into an algorithm to generate a score;
 comparing the score with a predetermined cutoff value; and
 identifying that the colon cancer in the subject is not completely removed when
 the score is equal to or greater than the predetermined cutoff value or identifying that the
 colon cancer in the subject is completely removed when the score is less than the
 predetermined cutoff value.

4. A method for evaluating the response of a subject having a colon cancer to a first therapy,
 the method comprising:

(1) at a first time point:

(a) determining the expression level of at least 14 biomarkers from a first test
 sample from the subject by contacting the first test sample with a plurality of
 agents specific to detect the expression of the at least 14 biomarkers, wherein the

14 biomarkers comprise *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, *UMPS*, and a housekeeping gene;

(b) normalizing the expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS*;

(c) inputting each normalized expression level into an algorithm to generate a first score;

(2) at a second time point, wherein the second time point is after the first time point and after the administration of the therapy to the subject:

(a) determining the expression level of at least 14 biomarkers from a second test sample from the subject by contacting the second test sample with a plurality of agents specific to detect the expression of the at least 14 biomarkers, wherein the 14 biomarkers comprise *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, *UMPS*, and the housekeeping gene;

(b) normalizing the expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *S100P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS*;

(c) inputting each normalized expression level into the algorithm to generate a second score;

(3) comparing the first score with the second score; and

(4) identifying that the subject is responsive to the first therapy when the second score is significantly decreased as compared to the first score or identifying that the subject is not responsive to the first therapy when the second score is not significantly decreased as compared to the first score.

5. A method comprising:
 - determining the expression level of at least 14 biomarkers from a test sample from a subject by contacting the test sample with a plurality of agents specific to detect the expression of the at least 14 biomarkers, wherein the 14 biomarkers comprise *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *SI00P*, *SNRPA*, *SORD*, *STOML2*, *UMPS*, and a housekeeping gene;
 - normalizing the expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *SI00P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS* to the expression level of the housekeeping gene, thereby obtaining a normalized expression level of each of *ADRM1*, *CDK4*, *COMT*, *DHCR7*, *HMOX2*, *MCM2*, *PDXK*, *POP7*, *SI00P*, *SNRPA*, *SORD*, *STOML2*, and *UMPS*;
 - inputting each normalized expression level into an algorithm to generate a score;
 - comparing the score with a predetermined cutoff value; and
 - administering a first therapy to the subject when the score is equal to or greater than the predetermined cutoff value.
6. The method of any one of claims 1-3 or 5, wherein the predetermined cutoff value is at least 50% on a scale of 0-100%.
7. The method of any one of claims 1-3 or 5, wherein the predetermined cutoff value is at least 60% on a scale of 0-100%.
8. The method of any one of claims 1-7, wherein the housekeeping gene is selected from the group consisting of *MRPL19*, *PSMC4*, *SF3A1*, *PUM1*, *ACTB*, *GAPD*, *GUSB*, *RPLP0*, *TFRC*, *MORF4L1*, *18S*, *PPIA*, *PGK1*, *RPL13A*, *B2M*, *YWHAZ*, *SDHA*, and *HPRT1*.
9. The method of any one of claims 1-8, wherein the housekeeping gene is *MORF4L1*.
10. The method of any one of claims 1-9, having a sensitivity greater than 85%.
11. The method of any one of claims 1-10, having a specificity greater than 85%.

12. The method of any one of claims 1-11, wherein at least one of the at least 14 biomarkers is RNA, cDNA or protein.
13. The method of claim 12, wherein when the biomarker is RNA, the RNA is reverse transcribed to produce cDNA, and the produced cDNA expression level is detected.
14. The method of claim 12, wherein the expression level of the biomarker is detected by forming a complex between the biomarker and a labeled probe or primer.
15. The method of any one of claims 1-4, wherein the predetermined cutoff value is derived from a plurality of reference samples obtained from subjects not having or not diagnosed with a neoplastic disease.
16. The method of claim 15, wherein the neoplastic disease is colon cancer.
17. The method of any one of claims 1-16, wherein the algorithm is XGBoost (XGB), Random Forest (RF), glmnet, cforest, Classification and Regression Trees for Machine Learning (CART), treebag, K-Nearest Neighbors (kNN), neural network (nnet), Support Vector Machine radial (SVM-radial), Support Vector Machine linear (SVM-linear), Naïve Bayes (NB), or multilayer perceptron (mlp).
18. The method of any one of claims 1-17, wherein the algorithm is XGBoost.
19. The method of any one of claims 1-3, further comprising administering to the subject a first therapy when the score is equal to or greater than the predetermined cutoff.
20. The method of claim 4, wherein the first time point is prior to the administration of the first therapy to the subject.

21. The method of claim 4, wherein the first time point is after the administration of the first therapy to the subject.
22. The method of claim 4, further comprising, continuing to administer the first therapy to the subject when the second score is significantly decreased as compared to the first score.
23. The method of claim 4, further comprising, discontinuing administration of the first therapy to the subject when the second score is not significantly decreased as compared to the first score.
24. The method of claim 4, further comprising administering a second therapy to the subject when the second score is not significantly decreased as compared to the first score.
25. The method of any one of claims 4 or 20-24, wherein the second score is significantly decreased as compared to the first score when the second score is at least 25% less than the first score.
26. The method of any one of claims 1-25, wherein the first therapy or the second therapy comprises anti-cancer therapy, surgery, chemotherapy, targeted drug therapy, radiation therapy, immunotherapy or any combination thereof.
27. The method of any one of claims 1-26, wherein when the first therapy or the second therapy comprises surgery, the surgery comprises removing a polyp during a colonoscopy, endoscopic mucosal resection, a partial colectomy, an ostomy, removing at least one cancerous lesion from the liver, or any combination thereof.
28. The method of any one of claims 1-26, wherein when the first therapy or the second therapy comprises chemotherapy, the chemotherapy comprises FOLFOX, FOLFIRI, a combination of 5-FU and leucovorin, capecitabine, irinotecan, CapeOx or any combination thereof.

29. The method of any one of claims 1-26, wherein when the first therapy or the second therapy comprises targeted drug therapy, the targeted drug therapy comprises bevacizumab, cetuximab, panitumumab, regorafenib, a combination of trifluridine and tipiracil, a EGFR TKI inhibitor or any combination thereof.
30. The method of any one of claims 1-26, wherein when the first therapy or the second therapy comprises anti-cancer therapy, the anticancer therapy comprises anti-colon cancer therapy.
31. The method of any one of claims 1-26, wherein when the first therapy or the second therapy comprises immunotherapy, the immunotherapy comprises pembrolizumab, nivolumab or a combination of pembrolizumab and nivolumab.